

The following Listing of Claims will replace all prior versions, and listings, of claims in the application:

**Listing of the Claims**

Claims 1-66 (canceled).

67. (New) A composition comprising a stabilized exendin-4 (1-39) comprising:
- (a) a deletion of 0 to 5 amino acids at positions corresponding to position 34-38 of exendin-4; and
  - (b) an alpha-aspartate (Asp) or beta-aspartate (isoaspartyl) residue at a position corresponding to the Asn residue at position 28 of exendin-4.
68. (New) The composition of claim 67 further comprising at least one of:
- (i) an oxidized methionine residue at a position corresponding to position 14 of exendin 4,
  - (ii) an oxidized tryptophan residue at a position corresponding to position 25 of exendin 4; and
  - (iii) a deamidated or hydrolyzed Gln at a position corresponding to position 13 of exendin 4.
69. (New) The composition of claim 67 or 68 further comprising at least one peptide sequence Z of 4-20 amino acid residues covalently bound to the stabilized exendin; or a pharmaceutically acceptable salt or solvate thereof.
70. (New) The composition of claim 68, wherein:
- (a) the oxidized methionine residue is a methioninyl sulfoxide or a methioninyl sulfone; and/or
  - (b) the oxidized tryptophan residue comprises an oxidized 3H-indol-3-yl group; and/or

- (c) the oxidized tryptophan residue is N-formylkynurenine (NFK), 3-hydroxykynurenine (3-OH-KYN), hydroxytryptophan (HTRP), or kynurenine (KYN).

71. (New) The composition of claim 67, wherein Z comprises between about 4 to about 20 Lys amino acid units.

72. (New) The composition of claim 69, wherein Z comprises 6 Lys amino acid units.

73. (New) The composition of claim 67, wherein the stabilized exendin-4 (1-39) compound and Z are bonded by a peptide bond.

74. (New) The composition of claim 67, wherein Z is covalently bound to the stabilized exendin-4 (1-39) compound at the C-terminal carbonyl function.

75. (New) The composition of claim 67, wherein the stabilized exendin-4 (1-39) compound comprises any one of the following sequences:

des Pro<sup>36</sup> [Asp<sup>28</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup> [IsoAsp<sup>28</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup> [Met(0)<sup>14</sup>, Asp<sup>28</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup> [Met(0)<sup>14</sup>, IsoAsp<sup>28</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup> [Trp(02)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup> [Trp(02)<sup>25</sup>, IsoAsp<sup>28</sup>]Exendin-4 (1-39) or  
des Pro<sup>36</sup> [Met(0)<sup>14</sup> Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup> [Met(0)<sup>14</sup> Trp(O<sub>2</sub>)<sup>25</sup>, IsoAsp<sup>28</sup>]Exendin-4 (1-39), or

76. (New) The composition of claim 75 further comprising the following group linked to the C-terminus of the compound: -Lys<sub>6</sub>-NH<sub>2</sub>.

77. (New) The composition of claim 67, wherein the stabilized exendin-4 (1-39) compound comprises any one of the following sequences:

H-(Lys)<sub>6</sub>- des Pro<sup>36</sup> [Asp<sup>28</sup>]Exendin-4(1-39)-Lys<sub>6</sub>-NH<sub>2</sub>  
 des Asp<sup>28</sup> Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> Exendin-4(1-39) -NH<sub>2</sub>,  
 H-(Lys)<sub>6</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Asp<sup>28</sup>]Exendin-4(1-39) -NH<sub>2</sub>  
 H-Asn-(Glu)<sub>5</sub> des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Asp<sup>28</sup>]Exendin-4(1-39) -NH<sub>2</sub>,  
 des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Asp<sup>28</sup>]Exendin-4(1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,  
 H-(Lys)<sub>6</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Asp<sup>28</sup>]Exendin-4(1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,  
 H-Asn-(Glu)<sub>5</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Asp<sup>28</sup>]Exendin-4(1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,

H-(Lys)<sub>6</sub>- des Pro<sup>36</sup> [Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(1-39)-Lys<sub>6</sub>-NH<sub>2</sub>,  
 H- des Asp<sup>28</sup> Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Trp(O<sub>2</sub>)<sup>25</sup>]Exendin-4(1-39) -NH<sub>2</sub>,  
 H-(Lys)<sub>6</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(1-39) -NH<sub>2</sub>,  
 H-Asn-(Glu)<sub>5</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(1-39) -NH<sub>2</sub>,  
 des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,  
 H-(Lys)<sub>6</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,  
 H-Asn-(Glu)<sub>5</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,

H-(Lys)<sub>6</sub>- des Pro<sup>36</sup> [Met(O)<sup>14</sup>, Asp<sup>28</sup>]Exendin-4(1-39)-Lys<sub>6</sub>-NH<sub>2</sub>,  
 des Met(O)<sup>14</sup> Asp<sup>28</sup> Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> Exendin-4(1-39) -NH<sub>2</sub>,  
 H-(Lys)<sub>6</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Met(O)<sup>14</sup>, Asp<sup>28</sup>]Exendin-4(1-39) -NH<sub>2</sub>,  
 H-Asn-(Glu)<sub>5</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Met(O)<sup>14</sup>, Asp<sup>28</sup>] Exendin-4(1-39) -NH<sub>2</sub>,  
 des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Met(O)<sup>14</sup>, Asp<sup>28</sup>]Exendin-4(1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,  
 H-(Lys)<sub>6</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Met(O)<sup>14</sup>, Asp<sup>28</sup>]Exendin-4(1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,  
 H-Asn-(Glu)<sub>5</sub> des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Met(O)<sup>14</sup>, Asp<sup>28</sup>]Exendin-4(1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,

H-Lys<sub>6</sub>- des Pro<sup>36</sup> [Met(O)<sup>14</sup>, Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(1-39)-Lys<sub>6</sub>-NH<sub>2</sub>,  
 H- des Asp<sup>28</sup> Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Met(O)<sup>14</sup>, Trp(O<sub>2</sub>)<sup>25</sup>]Exendin-4(1-39) -NH<sub>2</sub>,  
 H-(Lys)<sub>6</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Met(O)<sup>14</sup>, Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(1-39) -NH<sub>2</sub>,  
 H-Asn-(Glu)<sub>5</sub>- des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Met(O)<sup>14</sup>, Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(1-39) - NH<sub>2</sub>,  
 des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Met(O)<sup>14</sup>, Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,

H-(Lys)<sub>6</sub>-des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Met(O)<sup>14</sup>, Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(S1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,  
H-Asn-(Glu)<sub>5</sub>-des Pro<sup>36</sup>, Pro<sup>37</sup>, Pro<sup>38</sup> [Met(O)<sup>14</sup>, Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4(1-39)-(Lys)<sub>6</sub>-NH<sub>2</sub>,  
or a pharmaceutically acceptable salt or solvate thereof.

78. (New) The composition of claim 67, wherein the amino acid residues have an L-configuration, a D-configuration, or the composition includes a mixture of L- and D-amino acid residues.

79. (New) A composition of any one of claims 67, 68, or 70-78, further comprising a pharmaceutically acceptable carrier.

80. (New) A composition of claim 69, further comprising a pharmaceutically acceptable carrier.

81. (New) The composition of claim 79, wherein the composition comprises a depot formulation, microspheres, liposomes or the composition includes a stabilized liquid formulation.

82. (New) The composition of claim 80, wherein the composition comprises a depot formulation, microspheres, liposomes or the composition includes a stabilized liquid formulation.

83. (New) The pharmaceutically acceptable composition of claim 79, wherein the composition comprises at least one of the following compounds:

des Pro<sup>36</sup>[Asp<sup>28</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup> [IsoAsp<sup>28</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup>[Met(O)<sup>14</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup> [Trp(O<sub>2</sub>)<sup>25</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup> [Met(O)<sup>14</sup>, Asp<sup>28</sup>]Exendin-4 (1-39)  
des Pro<sup>36</sup> [Met(O)<sup>14</sup>, IsoAsp<sup>28</sup>]Exendin-4 (1-39),

des Pro<sup>36</sup>[Met(O)<sup>14</sup>, Trp(O<sub>2</sub>)<sup>25</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup>[Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup>[Trp(O<sub>2</sub>)<sup>25</sup>, IsoAsp<sup>28</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup>[Met(O)<sup>14</sup>, Trp(O<sub>2</sub>)<sup>25</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup>[Met(O)<sup>14</sup>, Trp(O<sub>2</sub>)<sup>25</sup>, Asp<sup>28</sup>]Exendin-4 (1-39),  
des Pro<sup>36</sup>[Met(O)<sup>14</sup>, Trp(O<sub>2</sub>)<sup>25</sup>, IsoAsp<sup>28</sup>]Exendin-4 (1-39), and

84. (New) The composition of claim 83 further comprising the following group linked to the C-terminus of the compound: -Lys<sub>6</sub>-NH<sub>2</sub>.

85. (New) A method of making the composition of claim 67, the method comprising at least one of the following steps:

- (a) obtaining exendin-4 (1-39) or a variant, analogue, or derivative thereof; and
- (b) incubating the exendin-4 (1-39) or the variant, analogue, or derivative thereof under conditions sufficient to introduce at least one of the following amino acids therein:  
an Asn residue having a deaminated side chain, an Asn residue having hydrolyzed side chain or a structural isomer of an Asp residue, wherein the Asn or Asp residue corresponds to position 28 of exendin-4.

86. (New) The method of claim 85, wherein the conditions introduce at least one of the following:

- (i) an oxidized methionine residue corresponding to position 14 of exendin-4,
- (i) an oxidized tryptophan residue corresponding to position 25 of exendin-4;  
and
- (iii) a deaminated or hydrolyzed Gln corresponding to position 13 of exendin-4.

87. (New) The method of claim 86 further comprising the step of detecting presence or absence of at least one of amino acids (i)-(iii).

88. (New) The method of claim 87, further comprising the step of identifying at least one of the amino acids (i)-(iii) in the composition.

89. (New) The method of claim 85, wherein the conditions include contact with at least one of water, heat, light, metal, metal ions, water vapor or oxygen.

90. (New) The method of claim 89, wherein the conditions further include contact with about room temperature (25°C).

91. (New). The method of claim 90, wherein the conditions further include contact with air.

92. (New) A method for treating diabetes type 1 or type 2, insulin resistance syndrome, impaired glucose tolerance (IGT), obesity, eating disorders, hyperglycemia, metabolic disorders, and gastric disease, the method comprising administering a therapeutically effective amount of the composition of claim 67.

93. (New) A method for treating disease states associated with elevated blood glucose levels, said method comprising administering a therapeutically effective amount of the composition of claim 67 or 68.

94. (New) A method for treating disease states associated with elevated blood glucose levels, said method comprising administering a therapeutically effective amount of the composition of claim 69.

95. (New) A method for regulation of blood glucose levels, the method comprising administering a therapeutically effective amount of the composition of claim 67 or 68.

96. (New) A method for regulation of blood glucose levels, the method comprising administering a therapeutically effective amount of the composition of claim 69.

97. (New) A method for regulation of gastric emptying, the method comprising administering a therapeutically effective amount of the composition of claim 67 or 68.

98. (New) A method for regulation of gastric emptying, the method comprising administering a therapeutically effective amount of the composition of claim 69.

99. (New) A method of stimulating insulin release in a mammal comprising administering an effective insulinotropic amount of the composition of claim 67 or 68.

100. (New) A method of stimulating insulin release in a mammal comprising administering an effective insulinotropic amount of the composition of claim 69.

101. (New) A method for treating any one of the following conditions: diabetes type 1 or type 2, insulin resistance syndrome, impaired glucose tolerance (IGT), obesity, eating disorders, 30 hyperglycemia, metabolic disorders, and gastric disease, disease states associated with elevated blood glucose levels, regulation of blood glucose levels, regulation of gastric emptying, stimulating insulin release, the method comprising administering to a mammal in need of such treatment, a therapeutically specific amount of the composition of claim 67 or 68.

102. (New) A method for treating any one of the following conditions: diabetes type 1 or type 2, insulin resistance syndrome, impaired glucose tolerance (IGT), obesity, eating disorders, 30 hyperglycemia, metabolic disorders, and gastric disease, disease states associated with elevated blood glucose levels, regulation of blood glucose levels, regulation of gastric emptying,